War on Drug Resistance: Policy Interventions to Tackle Antibiotic Misuse in Canada

by

Colin Bowbrick

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Name:	**Colin Bowbrick**
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Title:	***War on Drug Resistance: Policy Interventions to Tackle Antibiotic Misuse in Canada***
Examining Committee:	**Chair:** Doug McArthur Professor, School of Public Policy, SFU
	Dominique Gross Senior Supervisor Professor
	Nancy Olewiler Internal Examiner Professor
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Abstract

Antimicrobial resistance is a growing threat in Canada with profound implications for public health and wellbeing. Widespread misuse of antibiotics has led to increasing numbers of drug-resistant “superbugs” capable of causing serious and potentially untreatable infections. Addressing antibiotic misuse is crucial in order to curb antimicrobial resistance, but there is a lack of coordinated policy action across the country. Furthermore, research on the predictors of antibiotic misuse in Canada is sparse, which hinders policy makers’ ability to develop targeted interventions. This study analyzes national survey data to shed light on the extent of antibiotic misuse in Canada, including uncovering socio-demographic predictors of public misuse. The findings are used to inform proposed policy recommendations that aim to reduce antibiotic misuse in order to better position Canada to tackle antimicrobial resistance in the years ahead.

Keywords: Antimicrobial resistance; antibiotic misuse; predictors; antimicrobial stewardship; logistic regression

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AMR	Antimicrobial resistance
AMS	Antimicrobial stewardship
AMU	Antimicrobial use
CARSS	Canadian Antimicrobial Resistance Surveillance System
CIPARS	Canadian Integrated Program for Antimicrobial Resistance Surveillance
CPCSSN	Canadian Primary Care Sentinel Surveillance Network
CPE	Carbapenem-producing enterobacteriaceae
DDD	Defined daily dose
ESAG	Enhanced Surveillance of Antimicrobial-resistant Gonorrhea
FHT	Family Health Team
MRSA	Methicillin-resistant Staphylococcus aureus
PHAC	Public Health Agency of Canada
PMH	Patient Medical Home
STI	Sexually transmitted infection

Preface

As it currently sweeps the world, causing unprecedented strains on modern healthcare systems and the global economy, COVID-19 reminds us of the importance of recognizing infectious diseases as the potentially catastrophic public health threats they are. While this capstone was not written with pandemic preparedness in mind, many of the best practices associated with addressing antimicrobial resistance, such as robust surveillance networks and effective public health messaging, appear to be the same practices used by jurisdictions that have seen early success managing this crisis.

Fortunately, COVID-19 will eventually subside on its own regardless of what we do, but antimicrobial resistance (AMR) will continue to slowly grow in magnitude over the years and decades to come unless decisive action is taken. Although AMR is unlikely to grip the world in such a dramatic fashion, the lessons learned from COVID-19 should serve as a warning: It’s never a serious problem – until it suddenly is.

Chapter 1.

Introduction

Antibiotics are a type of medication that eliminate or slow the growth of bacteria and are widely used in modern medicine to treat bacterial infections. Since their discovery in the early 20th century, antibiotics have been responsible for saving millions of lives worldwide and are considered one of the most ground-breaking medical discoveries in history due to their ability to effectively cure previously untreatable infections. However, over the last several decades, the effectiveness of antibiotics has gradually declined, and bacteria are becoming increasingly resistant to antibiotic therapies.

Antimicrobial[1] resistance (AMR) is a naturally occurring evolutionary process in which microbes develop resistance to antimicrobial treatments, such as bacteria developing resistance to antibiotics. Extensive misuse of antibiotics has led to the emergence of resistant "superbug" strains of previously treatable infections. By 2050, AMR is projected to be responsible for 10 million deaths annually – more than the current number of deaths from cancer -- and will cost the global economy a cumulative total of $100 trillion (O'Neill, 2014). AMR is therefore widely considered to be one of the greatest global public health threats of the 21st century.

In Canada, AMR is a concern of national significance; it is estimated that 1 in 16 Canadians admitted to hospital will contract drug-resistant infections (Martin et al., 2019). Furthermore, it is estimated that AMR treatment procedures burden healthcare systems with an additional $10,000 - $40,000 per patient in costs (OECD, 2015). By 2050, resistant infections are projected to be responsible for approximately 400,000 deaths in Canada (Council of Canadian Academies, 2019). As a response to this growing public health issue, federal and provincial governments have launched a

[1] "Antimicrobial" is an umbrella term that is used to refer to agents that destroy microorganisms. These agents include antibiotics, antifungals, and antivirals, among others. However, the term "antimicrobial resistance" is often used interchangeably with "antibiotic resistance," as antibiotics are the agents most commonly implicated in resistance. For the purposes of this paper, the term "antimicrobial" is used interchangeably with "antibiotic" and does not refer to any other agents.

number of policy initiatives with the goal of surveying and containing the spread of AMR in Canada, including national action plans, antibiotic stewardship programs, and antimicrobial resistance surveillance systems.

Antibiotic misuse is one of the key driving factors behind the spread of AMR, and there is evidence that significant misuse occurs in Canada. Over-prescribing of antibiotics from healthcare practitioners is common (Silverman et al., 2017) and appears to be in line with over-prescribing rates in similar countries such as the United States (Chua, Fischer, & Linder, 2019). Additionally, public misuse and lack of knowledge of proper antibiotic use is also a concern in Canada (Leger, 2018), although there is a lack of Canadian literature on patient misuse.

The research focus of this study explores both the extent and predictors of antibiotic misuse in Canada using an analysis of national survey data. The findings of this analysis help to inform a number of policy options aimed at addressing antibiotic misuse, and the benefits and disadvantages of these options are analyzed and discussed using a set of criteria. Finally, recommendations are made based on this analysis, with the goal of reducing antibiotic misuse and, by extension, reducing the threat of AMR in Canada.

Chapter 2.

Antimicrobial Resistance

This chapter provides a definition of AMR and discusses the nature of its threat to public health. Notable AMR trends in both the global and Canadian contexts are also highlighted.

2.1 What is Antimicrobial Resistance?

AMR occurs when microorganisms evolve the ability to resist antimicrobials, rendering antimicrobial treatments ineffective. Bacteria reproduce rapidly and can therefore evolve at a much faster rate than humans and other animals. Antibiotics destroy bacteria and thus place selective evolutionary pressure on bacteria to adapt. Bacteria that by chance develop a mutation that makes them resistant to an antibiotic will be more likely to survive and therefore will be more likely to reproduce and pass on their advantageous resistance traits. Conversely, bacteria that do not possess these resistance traits are more likely to die off. Because of this, the resistant bacteria will proliferate and become increasingly common. This process by which bacteria evolve genetic resistance to antibiotics over time is referred to as AMR (O'Neill, 2014).

AMR presents a serious public health threat, as much of modern medicine relies on antibiotic therapy. Bacterial infections often require the use of antibiotics in order to treat effectively, particularly in populations with weakened immune systems such as infants, the elderly, and those with underlying medical conditions. Additionally, common medical procedures such as surgeries often require antibiotic prophylaxis – the administration of antibiotics prior to the procedure in order to reduce the risk of postoperative infections (Crader & Varacallo, 2019). Similarly, treatments such as chemotherapy sometimes require the prophylactic use of antibiotics to reduce the risk of infection, as chemotherapy can weaken the immune system of patients undergoing treatment. Thus, AMR both limits our ability to treat common bacterial infections and increases the risk of developing serious infections from medical procedures that increase patients' vulnerability to infection.

2.2 Global AMR Trends

Global data on AMR suggests that it is a widespread and growing issue around the world. AMR is currently estimated to be responsible for approximately 700,000 deaths globally every year and is projected to be responsible for 10 million deaths annually by 2050 (O'Neill, 2014). The World Bank estimates that AMR will exert a drag on global GDP of between 1.1% and 3.8% by mid-century based on current projections (Jonas et al., 2017). Bacterial resistance to antibiotics is reported in all countries around the world, although rates of resistance vary significantly from country to country. There are also significant limitations in estimating resistance rates globally due to lack of data availability.

Generally, the public health impacts of AMR are felt more acutely in poorer and developing countries, although this also varies depending on the type of bacteria. For example, Methicillin-resistant Staphylococcus aureus (MRSA) is a bacteria that is commonly implicated in skin and soft-tissue wound infections (Enright et al., 2002). It is one of the most prevalent drug-resistant infections around the world and is commonly reported in both developed and developing countries. MRSA rates vary from country to country, with resistance rates generally being somewhat higher for developing countries such as those in Southeast Asia, Africa, and South America. (The Center for Disease Dynamics, Economics & Policy, 2019).

However, for bacteria that tend to be more prevalent in developing countries such as E.coli, global resistance rates follow suit (The Center for Disease Dynamics, Economics & Policy, 2019). Overall, countries with a higher prevalence of infections from a particular type of bacteria are more likely to have higher rates of resistance for said bacteria. Poorer, developing countries tend to have higher rates of infections for most types of bacteria and thus experience higher rates of AMR generally.

2.3 AMR Trends in Canada

Developed countries such as Canada are not experiencing the public health impacts of AMR as acutely as developing countries; however, AMR remains a significant national public health issue. It is estimated that 1 in 16 hospitalized Canadians develop resistant infections every year (Martin et al., 2019), but there is little official tracking of

AMR-related infections and deaths in Canada. Other estimates have suggested that resistant infections were implicated in approximately 14,000 deaths in Canada in 2018 and are projected to be responsible for 400,000 cumulative deaths by the year 2050 (Council of Canadian Academies, 2019).

AMR places a significant burden on the Canadian economy as well. Currently, overall resistance to first-line antibiotics[2] is at 26% and is likely to reach 40% by 2050 (Council of Canadian Academies, 2019). A 40% resistance rate is projected to reduce Canada's GDP by $21 billion per year. In 2018, longer hospital stays and treatments associated with AMR cost the Canadian healthcare system $1.4 billion, with costs growing to $8 billion per year in 2050 if a 40% resistance rate to first-line antimicrobials were to be realized (Council of Canadian Academies, 2019).

AMR can increase the mortality and morbidity of a host of different bacterial infections, with some being more serious from a public health perspective than others. The subsections below briefly summarize some of the resistance trends of concern in Canada using national data from the Canadian Antimicrobial Resistance Surveillance System (CARSS).

2.3.1 Carbapenemase-producing enterobacteriaceae (CPE)

Carbapenems are a class of antibiotics that remain highly effective for treating severe and high-risk bacterial infections (Papp-Wallace, Endimiani, Taracila, & Bonomo, 2011). Because of their effectiveness, their use is typically reserved for highly resistant bacterial infections, making them a last-resort class of antibiotics in Canada. Since 2009, the proportion of lab-tested bacteria isolates that have developed resistance to carbapenems has been rising (PHAC, 2018). These bacteria are referred to as carbapenemase-producing Enterobacteriaceae (CPE), and infections resulting from CPEs typically have limited treatment options.

[2] Classes of antibiotics are considered first-line treatments somewhat arbitrarily, but factors such as the availability, cost, and side effect profiles of antibiotics usually factor in. Antibiotics that are relatively accessible, cheap, and have few side effects are typically considered first-line antibiotics.

Rates of CPE infection remain very low, at 0.03 cases per 10,000 patient-days in 2017 and have not changed since 2012. However, CPE colonization[3] rates have increased five-fold since 2014, from 0.03 cases per 10,000 patient-days in 2014 to 0.14 in 2017. The mortality rate for those who develop an infection from CPEs was 19% between 2012 and 2017. While still rare, CPEs are capable of transferring resistance properties to other bacteria, which magnifies their public health threat.

2.3.2 Methicillin-resistant staphylococcus aureus (MRSA)

MRSA is a type of staphylococcus bacterium that is multi-drug resistant, meaning that it has developed resistance to several antibiotic classes. This reduces the number of treatment options for MRSA. It has historically been contracted in hospital settings, primarily in the form of soft tissue infections; however, over the last decade a new strain has emerged in the community known as community-associated MRSA (CA-MRSA) (Khawcharoenporn, Tice, Grandinetti, & Chow, 2010). Because it is often implicated in soft tissue infections, certain subpopulations are more at risk for MRSA infection. These subpopulations include children, athletes of contact sports, military personnel, and injection drug users (Khawcharoenporn, Tice, Grandinetti, & Chow, 2010).

Figure 1 illustrates the trend of MRSA infections from 2012 to 2017. MRSA infection rates overall have risen 13% over the last five years, from 2.8 cases per 10,000 patient-days in 2012 to 3.17 in 2017. This increase has occurred despite a 6% decrease in healthcare-associated MRSA infections. A 62% increase in community-associated MRSA infections is driving this trend, indicating that more people are starting to acquire infections in the community rather than in hospitals.

[3] Colonization of CPE refers to the presence of CPEs on a body surface (i.e. skin, mouth, airways) without causing disease.

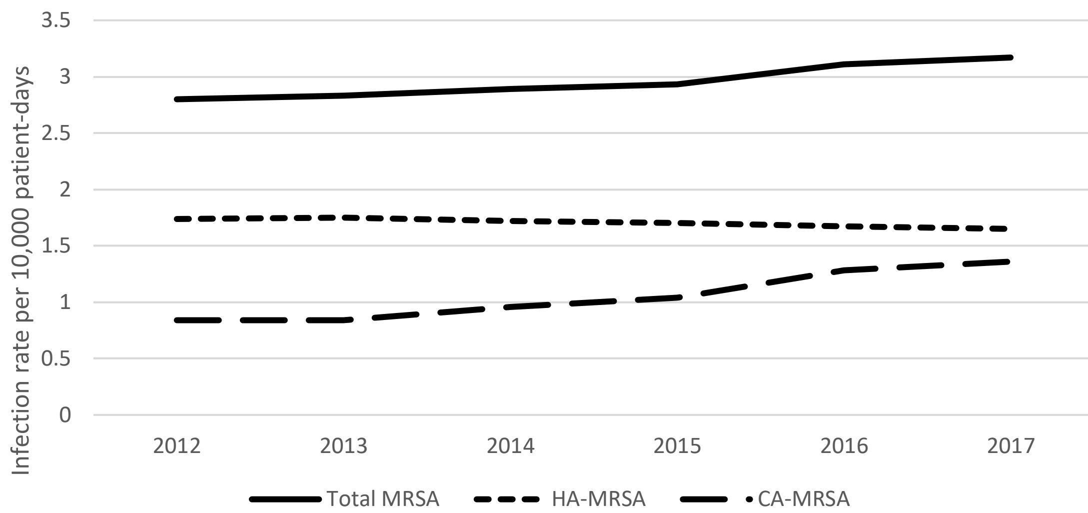

Figure 1. **Rate of healthcare-associated (HA) and community-associated (CA) MRSA infections, 2012-2017**

Source: PHAC (2018)

2.3.3 Neisseria gonorrhoeae

Neisseria gonorrhoeae is the bacteria that causes the sexually-transmitted infection (STI) known as gonorrhea (PHAC, 2018). Left untreated, gonorrhea can lead to serious and permanent health problems in both men and women. In women, gonorrhea can spread to the uterus or fallopian tubes and cause pelvic inflammatory disease, which can potentially lead to infertility (Svensson, Westrom, Ripa, & Mardh, 1980). Infertility can also result in men if gonorrhea is left untreated and can potentially spread to the blood causing a life threatening condition in both sexes (Holmes, Counts, & Beaty, 1971). Antibiotic regimens are used to fully treat and cure gonorrhea.

Gonorrhea is the second most common STI in Canada with over 19,000 cases reported in 2015, and infection rates have climbed substantially over the last several years (PHAC, 2019). Between 2010 and 2015, gonorrhea infection rates increased by 65.4%, from 33.5 cases per 100,000 population to 55.4 (Choudhri et al., 2018). Males, adolescents, and young adults are at significantly higher risk of contracting gonorrhea in Canada.

Gonorrhea has steadily become increasingly resistant to recommended antibiotic treatment regimens. According to PHAC's Enhanced Surveillance of Antimicrobial-resistant Gonorrhea (ESAG) program, 60% of Neisseria gonorrhoeae isolates were resistant to one or more antibiotics in 2015 – up from 55.2% of isolates in 2014 (PHAC, 2019). In 2013, an increase in resistance to the previous recommended antibiotic regimen prompted Canada to adopt a combination therapy of multiple antibiotics simultaneously. This combination therapy is still largely effective, but treatment failures have been reported in Australia and the United Kingdom (PHAC, 2019).

Chapter 3.

Antimicrobial Misuse in Canada

There are a number of key driving factors that contribute to AMR in Canada. One of the most critical factors is antimicrobial misuse. Antimicrobial misuse can occur in a variety of different ways involving both the general public and healthcare practitioners. Generally, there are two broad categories of antimicrobial misuse: over-prescribing and patient misuse. This chapter will explore the different manifestations of misuse and the extent to which misuse occurs in the country.

3.1 Over-prescribing

Over-prescribing occurs when healthcare practitioners engage in inappropriate healthcare prescribing practices, such as prescribing an antibiotic for a patient who does not have a bacterial infection. Viruses, for example, are common sources of infection but do not respond to antibiotic therapy. Over-prescribing contributes to AMR by exposing healthy bacteria to antibiotics unnecessarily, which places selective evolutionary pressure on bacteria to adapt -- increasing the likelihood of bacteria evolving resistance traits.

It is generally difficult to collect data on over-prescribing, as doing so would require follow-up diagnostics with patients who were prescribed antibiotics in order to determine whether a bacterial infection was indeed present. However, a study in the United States found that 23% of outpatient prescriptions were inappropriate, with an additional 35% being deemed potentially inappropriate (Chua, Fischer, & Linder, 2019). Another US study found similar findings, estimating that 40% of antibiotics filled by older adults were potentially inappropriate (Olesen et al., 2018). Canadian healthcare professionals have noted that these are reasonable estimates of over-prescribing in Canada as well (Mercer, 2019), and an Ontario study indicated that 46% of seniors with a non-bacterial infection were prescribed antibiotics (Silverman et al., 2017).

The responsibility of antibiotic prescribing as a whole falls predominantly on healthcare professionals in community settings, such as family clinics. While some antibiotics are prescribed in hospital settings, most are not; 92% of prescriptions are dispensed in the community, and family physicians are responsible for 65% of all prescriptions in Canada (PHAC, 2018). National CARSS data indicates that the overall prescription rate for antibiotics in Canada has remained steady over the last several years, at roughly 20 defined daily doses (DDDs) per 1,000 inhabitant-days. This equates to roughly 2% of the Canadian population receiving an antimicrobial on a typical day, with an estimated annual expenditure of approximately $822 million (PHAC, 2018). If an estimated 20%-40% of antibiotics are prescribed inappropriately, that would equate to roughly $165-$330 million of expenditures for unnecessary antimicrobials.

It is also worth noting that community antimicrobial prescription rates vary significantly across the country. Figure 2 illustrates antimicrobial prescription rates by province in 2017. Antimicrobial prescription rates were lowest in British Columbia, Quebec, and the territories, while rates were highest in the Atlantic provinces. Thus, antibiotic over-prescribing may also vary regionally in Canada as well, although it is worth noting that this discrepancy could be partially explained by demographic differences between provinces.

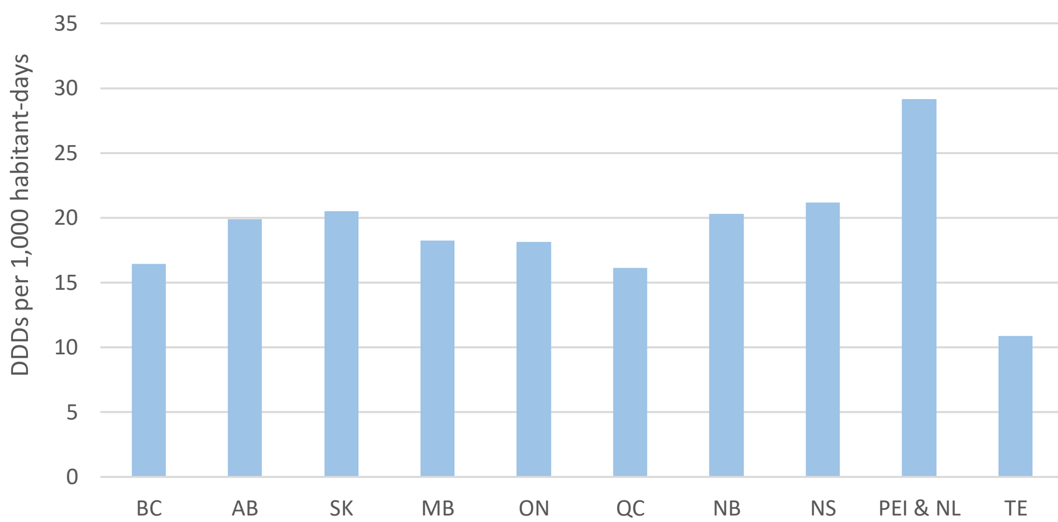

Figure 2. Regional distribution of defined daily doses (DDDs) per 1,000 inhabitant-days, community dispensation, 2017

Source: PHAC, 2018

3.1.1 Prescriber characteristics

The literature suggests that some of the variables that predict over-prescribing are prescriber characteristics. Silverman et al.'s Ontario study (2017) found that patients were more likely to receive antimicrobial prescriptions from mid- and late-career physicians than early-career physicians, potentially indicating that older physicians are less likely to adopt antimicrobial stewardship[4] (AMS) recommendations that have arisen in the last several years. Patients were also more likely to receive prescriptions from physicians trained outside of Canada, the United States, and the United Kingdom as antimicrobial stewardship may be emphasized less in certain countries. Finally, patients in the study were also more likely to receive prescriptions from physicians who saw over 25 patients per day than from physicians who saw fewer than 25 patients per day, suggesting that physicians who have higher patient volumes are more likely to prescribe antimicrobials in order to get through longer patient queues faster.

Additionally, prescriber habits and tendencies also appear to predict antimicrobial prescribing. A study of physicians prescribing antibiotics to residents in long-term care facilities in Ontario found that prior prescribing tendency was a significant predictor of current practice (Daneman et al., 2017). Historical tendencies predicted the start of antibiotic treatment, use of prolonged treatment duration, and antibiotic class selection.

3.1.2 Patient-physician interactions

While prescriber factors seem to be the predominant predictors for over-prescribing in community settings, patient behaviours and expectations also play a significant role. In physician-patient interactions, physicians report that fear of patient dissatisfaction is one of the most influential factors for antibiotic prescribing (Rodrigues et al., 2013). Many physicians reported that they believed patients expected an antibiotic prescription during their visit and therefore prescribed an antibiotic in order to maintain a positive relationship with their patients.

Patients are also more likely to be prescribed an antibiotic if they do not show a preference for shared decision-making (Deschepper et al., 2008). Patients who are involved in the decision-making process and see themselves as equal to their physician

[4] Antimicrobial stewardship is the practice of minimizing the emergence of AMR by using antibiotics only when necessary and, if needed, by selecting the appropriate antibiotic at the right dose, frequency, and duration to optimize outcomes.

tend to have views on and usage of antibiotics most in line with medical recommendations.

3.2 Patient Misuse

Apart from the behaviours patients engage in that can influence over-prescribing, patients also engage in other behaviours that are more directly associated with antimicrobial misuse. These behaviours involve the personal misuse of antibiotics. Some examples of misuse behaviours include failing to follow an antibiotic prescription as directed, inappropriately disposing of leftover antibiotics, self-medicating, and sharing personal prescriptions with others. Similar to over-prescribing, such behaviours can expose bacteria to antibiotics unnecessarily and facilitate the development of AMR.

There is little research on patient antimicrobial misuse in Canada. It is difficult to assess on a large scale whether patients are engaging in misuse behaviours in private once they receive an antibiotic prescription. However, one of the strongest predictors of antibiotic misuse is awareness of AMR and the public health risks associated with it (Norris et al., 2010). A national survey found that only 29% of Canadians consider themselves “somewhat” or “very” knowledgeable about AMR and ranked AMR among conditions that were of least concern (Leger, 2018). Additionally, 81% of respondents indicated a desire for more government information on AMR. A lack of public awareness of AMR can lead to antimicrobial misuse behaviours, as patients may be unaware of the proper guidelines for taking antibiotics or do not recognize the importance of following them.

Chapter 4.

Policy Problem and Stakeholders

The policy problem examined in this capstone is that antimicrobial misuse is contributing to the spread of antimicrobial resistance in Canada, causing an increasing number of Canadians to develop resistant infections.

Certain types of bacteria are developing resistance to antibiotics at a concerning rate, and the resistant infections they cause place both a public health and economic burden on Canada. Antibiotic misuse is a key driving factor behind AMR, and the literature in Canada suggests that Canadians are broadly uninformed of the threat of antimicrobial resistance and misuse, which may lead to behaviours consistent with patient misuse. Literature from other countries has indicated that certain socio-demographic characteristics are predictive of antibiotic misuse, although such studies are lacking in Canada. Determining whether these findings hold true in the Canadian context is important in order to better understand the policy problem.

As described in the previous chapter, there is also evidence of over-prescribing in Canada, as healthcare professionals such as physicians can often prescribe antibiotics inappropriately. Inappropriate prescriptions can include prescribing an antibiotic for a viral infection, in which case it would have no effect, or providing an antibiotic prescription for a bacterial infection that does not adhere to recommended treatment guidelines. Both over-prescribing and patient misuse fall under the broader category of antibiotic misuse. Therefore, the policy options considered will attempt to address both public misuse and over-prescribing to varying degrees, with a greater emphasis on over-prescribing as prescribers function as gatekeepers for antibiotic prescriptions in Canada.

Since the public health threats of antimicrobial resistance affect virtually everyone, it is accurate to say that the general public is an important stakeholder group. However, AMR tends to impact certain populations disproportionately more than others. Seniors, low-income families, and those living in rural communities are often more heavily impacted by AMR, as they tend to either have poorer access to healthcare or inherently poorer health outcomes associated with infections. Additionally, healthcare professionals are also important stakeholders, as they play a critical role in prescribing antibiotics as well as treating resistant infections in the healthcare system.

Chapter 5.

Methodology

This chapter outlines the methodology that is used to shed light on the policy problem and help inform policy analysis. The primary methodology is a quantitative analysis of Statistics Canada survey data using descriptive statistics and logistic regression analysis to better understand antibiotic misuse in Canada. The secondary methodology is a review of the literature to compare to the findings of this analysis.

5.1 Survey Analysis

The data source used for this analysis is the 2018 Canadian Community Health Survey (CCHS). The 2018 iteration of the survey includes an Antimicrobial Use (AMU) Rapid Response module asking participants about antibiotic use (see Appendix A for a list of Rapid Response AMU questions used in this analysis). This data source was accessed through one of Statistics Canada's Research Data Centres. Bootstrap weights obtained from Statistics Canada were used to account for the complex survey design of the CCHS in order to produce more accurate estimates of variance and statistical significance. Survey weights were also incorporated to extrapolate to the broader Canadian population. The data analysis involved a combination of descriptive statistics and multivariate logistic regression analysis.

5.1.1 Descriptive statistics

Descriptive statistics were used to provide proportion estimates of antibiotic use behaviour among the general population at the national and provincial levels. National proportion estimates are reported for three categories of variables: prescriber characteristics, prescription adherence, and prevalence of antibiotic leftovers/methods of leftover disposal.

Prescriber characteristics include the location antibiotics were reportedly prescribed from, as well as whether survey respondents reported receiving directions on how to take their antibiotic prescription properly. Prescription adherence includes the proportion of respondents who reported that they followed their prescription as directed.

Prevalence of antibiotic leftovers represents the proportion of respondents who received an antibiotic prescription and reported having leftovers remaining, while methods of leftover disposal are the ways in which participants chose to discard (or not discard) any leftover antibiotics that they had.

5.1.2 Regression analysis

A multivariate logistic regression analysis is conducted to identify predictors for two dependent variables. The first dependent variable is whether Canadians reported having leftover antibiotics from a prescription (yes vs. no). The second is whether Canadians who did have antibiotic leftovers returned them to the pharmacy (yes vs. no). Leftover antibiotics are used in this analysis as a proxy for antibiotic misuse, as having leftover antibiotics indicates that patients may not have followed their prescription appropriately, and the presence of leftover antibiotics can increase the likelihood of further misuse via behaviours such as self-medication.

Based on a review of the literature and the available variables in the CCHS, five socio-demographic independent variables are hypothesized to have an effect on both dependent variables. These included gender (male vs. female), age (per year increase), immigrant status (immigrant vs. non-immigrant), education (post-secondary completion vs. secondary completion or lower), and income (per $10,000 salary increase). Additionally, prescriber type (dentist’s office vs. walk-in clinic/doctor’s office) is included as well based on the growing proportion of antibiotic prescriptions originating from dentistry (CARSS, 2017).

Table 1 outlines the hypotheses for the nature of the effect of the explanatory variables on both the likelihood of having leftovers and the likelihood of returning antibiotics to the pharmacy. Variables that are significant predictors for having leftovers are expected to also be significant predictors for returning leftover antibiotics to the pharmacy.

Table 1. Explanatory variables and hypotheses

Explanatory Variable	Hypothesis
Gender (female vs. male)	H_0: AOR ≥ 1 H_A: AOR < 1
Age (per year older)	H_0: AOR ≥ 1 H_A: AOR < 1
Immigrant status (yes vs. no)	H_0: AOR ≤ 1 H_A: AOR > 1
Education level (post-secondary vs. secondary or less)	H_0: AOR ≥ 1 H_A: AOR < 1
Household income (per $10,000 increase)	H_0: AOR ≥ 1 H_A: AOR < 1
Prescriber type (dentist's office vs. walk-in clinic/doctor's office)	H_0: AOR ≤ 1 H_A: AOR > 1

5.2 Literature Review

A literature review was conducted to identify the explanatory variables that would potentially have an effect on the dependent variables in the survey analysis. The findings from the survey analysis are compared and discussed in the context of broader academic literature on this subject. While there is a lack of literature on predictors for behaviour with respect to leftover antibiotics, there is a significant amount of literature exploring antibiotic misuse behaviours more broadly. The literature includes both Canadian studies as well as studies in other countries.

Chapter 6.

Survey Analysis

This chapter presents a summary of results and a discussion of the findings from the survey analysis of the 2018 AMU Rapid Response CCHS. Data analysis was conducted using Stata 15 and Excel.

The total number of participants who responded to the CCHS AMU Rapid Response module was 27,446. Questions pertaining to AMU were restricted to participants who reported receiving an oral antibiotic prescription in the last 12 months (n=5,027) (See Appendix B for detailed sample characteristics). Statistics Canada employs survey techniques such as clustering and stratification in order to ensure respondent profiles are representative of the broader Canadian population. Thus, the survey sample is assumed to be generalizable.

Using the bootstrap and survey weights that were accompanied with the CCHS, estimates for the broader Canadian population were calculated. Thus, all proportions, odds ratios, and other figures reported below are based on weighted estimates for the total Canadian population and not of the samples themselves.

6.1 Antibiotic Use

Overall, 25.2% of Canadians reported receiving an antibiotic prescription in the past 12 months. The following section explores general survey results pertaining to reported prescriber characteristics, prescription adherence, prevalence of antibiotic leftovers, and methods of leftover disposal.

6.1.1 Prescriber characteristics

Figure 3 shows the locations from which Canadians received their antibiotic prescriptions. The majority of prescriptions were received from walk-in clinics or doctors' offices (69.3%), which aligns closely with other national figures (CARSS, 2017). Hospitals were the second most common location that Canadians received antibiotic prescriptions from, with a combined total of 16.2% of Canadians reporting receiving oral antibiotics from hospitals while admitted or as an outpatient. Of particular note is the proportion of prescriptions received from dentist offices, which accounted for 11.6% of all prescriptions in 2018. In 2015, antibiotic prescriptions from dentists accounted for less than 8% of total prescriptions (CARSS, 2017), indicating that the proportion of prescriptions associated with dental care may be on the rise. This trend has been observed in Canada for the last several years (Marra et al., 2016).

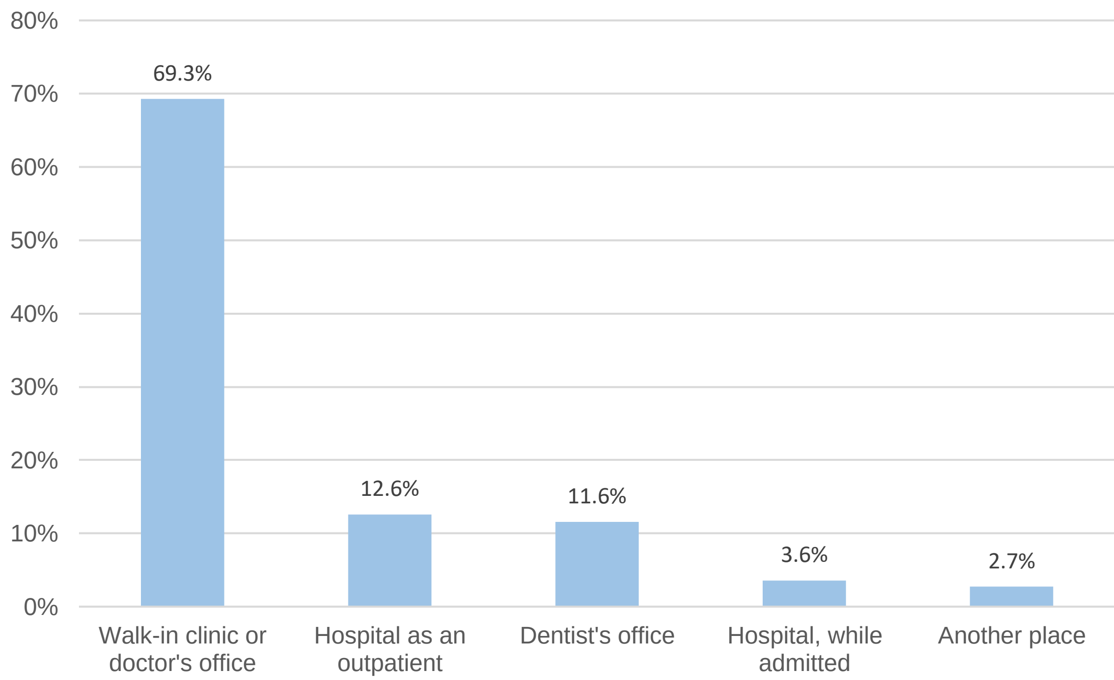

Figure 3. Location antibiotic prescription was received

Additionally, of the respondents who received an antibiotic prescription in the past year, 9.1% indicated that they did not receive any information from a healthcare professional on how to take their prescription. This lack of prescription direction from prescribers could partially explain why a similarly sized portion of respondents report having leftover antibiotics, as patients' understanding of treatment duration relies heavily on consultation from healthcare professionals.

6.1.2 Prescription adherence

Of those who received an oral antibiotic prescription in the prior 12 months, only 2.1% responded "no" to the question: "Did you take it as prescribed?" 94.1% indicated that they did take the antibiotics as prescribed. This suggests that the vast majority of

Canadians report that they take antibiotics properly, although there may be reasons to be wary of this result. Firstly, another recent national Canadian survey has indicated a significantly higher proportion of reported misuse among the Canadian public, with 21% of respondents reporting that they had stopped using antibiotics before the prescription was finished and 15% reporting that using leftover antibiotics to treat a new symptom or illness (Leger, 2018).

This discrepancy may be due to questionnaire design differences. The CCHS directly asks participants whether they took their antibiotic prescription as prescribed, whereas other surveys in the literature often forego this direct question and ask participants about specific behaviours associated with misuse. This discrepancy may be due to the fact that respondents may not fully understand what it means to follow a prescription properly.

6.1.3 Leftover antibiotics

While 94.1% of Canadians reported following their prescription properly, 15.3% reported having leftover antibiotics from their prescriptions in the past 12 months. This could indicate that a sizable proportion of the public stopped taking their prescription once they started feeling better but did not realize this constituted as following their prescription improperly. However, it is worth noting that an individual may have leftover antibiotics for other reasons, such as receiving an inappropriate antibiotic prescription from their prescriber. If an antibiotic was prescribed for a viral infection and the patient's symptoms resolved on their own shortly afterwards, then the likelihood of having leftover antibiotics increases.

Figure 4 shows the methods of disposal undertaken by Canadians who reported having leftover antibiotics. 60.0% of those with leftover antibiotics reported keeping them, while only 13.3% reported returning them to the pharmacy – the course of action most recommended by health bodies and professionals when in possession of leftover antibiotics. Combined, 16.5% of Canadians reported disposing of them by flushing them down the toilet/sink or by throwing them in the garbage.

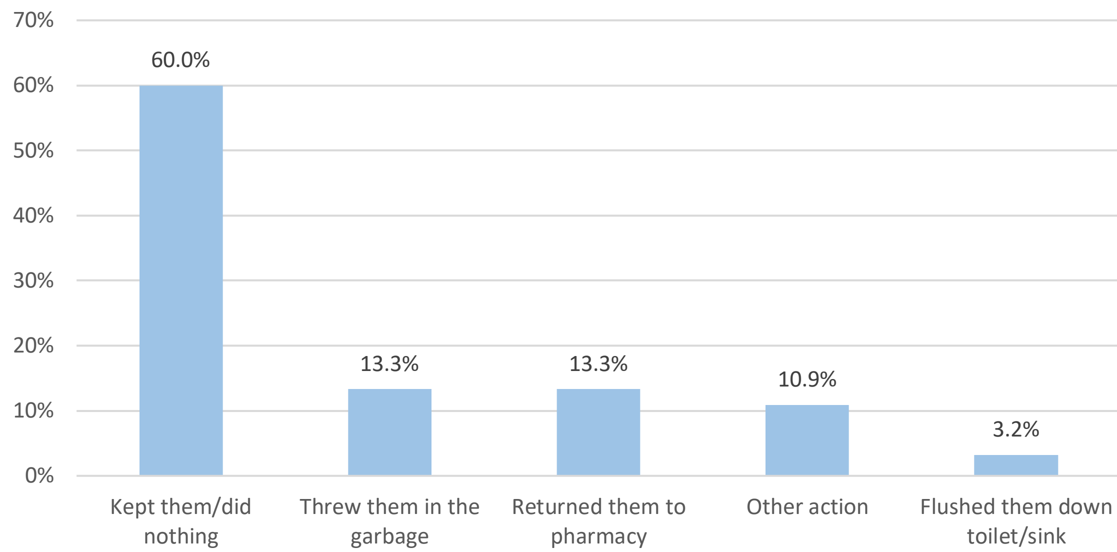

Figure 4. Action taken to dispose of leftover antibiotics

This suggests that the vast majority of Canadians who have leftover antibiotics do not return them to the pharmacy, with most opting to keep their leftovers or dispose of them an alternative way. This is a concern, as disposing of antibiotics improperly can unnecessarily expose bacteria in natural environments to small doses of antibiotics and facilitate AMR (Zarei-Baygi et al., 2019). Furthermore, keeping antibiotics instead of disposing of them is associated with an increased likelihood of using them inappropriately, such as by using leftovers to self-medicate when sick (Grigoryan et al., 2010).

6.2 Logistic Regression Analysis

A total of 5,027 respondents were included in the first analysis identifying predictors for having leftover antibiotics. 676 respondents were included in the second analysis of predictors for returning leftover antibiotics to the pharmacy. Adjusted odds ratios (AOR)[5] were calculated for the six explanatory variables to determine the nature of

[5] An odds ratio (OR) represents the odds of an outcome occurring when a condition is present versus when that condition is absent. ORs are used when the dependent variable is binary rather than continuous. For example, if a dependent variable was whether people vote in elections (yes vs. no) and a study was interested in examining whether gender (male vs. female) can predict if a person decides to vote, then an OR would likely be calculated. The OR would describe the odds of deciding to vote in an election when comparing males to females. If being male is the conditional category of interest and female is the reference category, then an OR of 0.8 would be interpreted as the odds of a male voting in an election are 0.8x the odds of a female voting in an election.

their effect on both dependent variables. All tests of significance were two-sided and a $p<0.05$ was selected for defining statistical significance. The results from the multivariate regression analysis are displayed in Table 2 (Raw Stata outputs can be seen in Appendix C).

Table 2. Multivariate logistic regression results

Characteristic	Received oral antibiotic prescription in past 12 months (n=5,027)		Had leftover oral antibiotics in past 12 months (n=676)	
	Had leftover oral antibiotics in past 12 months		Returned leftover oral antibiotics to pharmacy	
	AOR[6] (95% CI)	p-value	AOR (95% CI)	p-value
Gender (female vs. male)	0.60 (0.43 – 0.83)	0.002	5.40 (2.50 – 11.67)	<0.001
Age (per year older)	0.98 (0.97 – 0.99)	<0.001	1.02 (0.50 – 1.35)	0.127
Immigrant status (immigrant vs. non-immigrant)	0.64 (0.44 – 0.91)	0.013	0.50 (0.13 – 2.01)	0.331
Education (post-secondary vs. secondary or less)	0.80 (0.58 – 1.10)	0.173	0.62 (0.22 – 1.75)	0.362
Household Income (per $10,000 increase)	0.97 (0.92 – 1.02)	0.238	1.01 (0.88 – 1.16)	0.879
Prescriber type (dentist's office vs. walk-in clinic/doctor's office)	1.50 (1.07 – 2.10)	0.020	0.61 (0.25 – 1.49)	0.281

A total of four explanatory variables had a statistically significant effect on whether Canadians who received an antibiotic prescription had leftovers. Gender, age, and prescriber type all had effects and directionality consistent with the hypothesized effects in Table 1. However, while immigrant status was hypothesized to be significant, the directionality of its effect appears to contradict the original hypothesis; immigrants were less likely to report having leftover antibiotics than non-immigrants (AOR = 0.64,

[6] An adjusted odds ratio (AOR) is an OR that takes into account the effect of other explanatory variables in the regression. Therefore, the AORs in Table 2 are the ORs of each variable while taking into account the effects of the other five explanatory variables.

95% CI: 0.44-0.91). Furthermore, household income and education level were hypothesized to be significant, but were not.

As expected, being female had a statistically significant effect on the odds of having leftover antibiotics (AOR = 0.60, 95% CI: 0.43-0.83). The odds of a Canadian woman having leftover antibiotics after receiving a prescription are significantly less than the odds of a Canadian man having leftovers. This suggests that women are more likely to follow their prescription as directed than men.

Age also had a significant effect on the odds of having leftover antibiotics, with odds decreasing by 2% per every year older (AOR = 0.98, 95% CI: 0.97-0.99). This suggests that while seniors receive significantly more antibiotics than their younger counterparts in Canada, they are less likely to have leftovers – indicating that they may be more likely to follow their prescription as directed.

Finally, prescriber type had a significant effect on the odds of having leftover antibiotics as well. Canadians who received their prescription from a dentist's office had greater odds of having leftovers than those who received their prescription from a walk-in clinic or doctor's office (AOR = 1.50, 95% CI: 1.07-2.10). There may be a number of explanations for this, such as Canadians simply not treating an antibiotic prescription for dental purposes the same as they would an antibiotic prescription for more conventional medical purposes. Additionally, it may be the case that prescriptions from dentists are not accompanied with the same level of instruction on how to take the antibiotic as prescriptions from physicians, since antimicrobial stewardship programs and responsible prescribing practices have often focused on clinics and significantly less so on the field of dentistry. It is worth noting that there are other types of prescribers beyond clinics and dental offices, as illustrated in Figure 3. Future research may wish to compare additional prescriber types.

While gender, age, immigrant status, and prescriber type all had significant effects on whether Canadians reported having leftover antibiotics and were hypothesized to have an effect on whether Canadians returned antibiotics to the pharmacy, only gender had a statistically significant effect (AOR = 5.40, 95% CI: 2.50-11.67). As expected, females had greater odds returning any antibiotic leftovers to the pharmacy than males. Coupled with the previous finding, this suggests that women are both more likely to return leftover antibiotics to the pharmacy and less likely to have leftover antibiotics in the first place.

Household income and education level were also hypothesized to have an effect on likelihood of returning antibiotics to the pharmacy but were not statistically significant. The lack of significant variables with respect to the tendency to return antibiotics to the pharmacy may be in part due to the relatively small sub-sample (n=676) and larger confidence intervals for each variable.

6.3 Summary of Findings

The findings of this analysis show that a quarter of Canadians have received an antibiotic prescription in the past 12 months and that the vast majority of Canadians believe they took their antibiotics as prescribed (94.1%). However, roughly 15% of Canadians who were prescribed an antibiotic reported having leftovers, potentially indicating that Canadians are not necessarily sure what constitutes prescription adherence. The presence of leftover antibiotics could also be partially due to inappropriate prescribing as well. Furthermore, only 13% of Canadians who had leftovers returned them to the pharmacy, with 60% of Canadians keeping their leftovers. This presents a concern, as keeping antibiotics can increase the likelihood of other forms of antibiotic misuse.

Most Canadians reported receiving their antibiotic prescriptions from a walk-in clinic or doctor’s office, but roughly 12% of Canadians reported receiving their prescription from a dentist’s office. This is notable, in that the proportion of Canadians who receive prescriptions from dentists appears to be rising in Canada when comparing these findings to previous estimates (CARSS, 2017; Marra et al., 2016).

This analysis uncovered several significant predictors for having leftover antibiotics. Females, older Canadians, and immigrants are less likely to have leftover antibiotics following their prescription, whereas individuals who received their antibiotic prescription from a dentist’s office (vs. a doctor’s office) were more likely to report having leftovers. Gender was also a significant predictor for returning leftover antibiotics to the pharmacy, with females significantly more likely than males to do so. Contrary to expectation, household income and education level were not statistically significant predictors of either having leftovers or returning leftovers to the pharmacy.

Taken together, these findings help provide a demographic profile of Canadians who may be more likely to follow their prescriptions improperly and by extension potentially engage in other forms of antibiotic misuse. Specifically, young men are a broad demographic group that interventions aiming to reduce public antibiotic misuse may wish to target. Additionally, despite findings in other countries, immigrants in Canada do not seem to be at risk of having leftover antibiotics and engaging in misuse. In fact, this demographic group appears to be less likely to do so based on this analysis.

Prescriber type appears to be predictive of having leftover antibiotics as well. Canadians who received their prescriptions from dentists were more likely to report having leftovers than those who received their prescriptions from doctors. Coupled with the finding that a growing proportion of prescriptions are originating from dental offices, this suggests that increased attention should be placed on dentistry in Canada when implementing antimicrobial stewardship initiatives. Finally, almost 1/10 Canadians reported that they did not receive instructions on how to take their antibiotic prescription from healthcare professionals, which can also increase the likelihood of patient misuse.

6.4 Limitations

As mentioned earlier, while the presence of leftover antibiotics can be indicative of patient misuse, it can also be indicative of over-prescribing if the prescription was prescribed for a viral infection or did not otherwise follow recommended prescription guidelines. This analysis can describe the extent of leftover antibiotics in Canada and determine some of the predictors for having leftover antibiotics, but it cannot distinguish whether patient misuse or over-prescribing is responsible for the presence of leftovers. Most likely, it is some combination of both factors. However, the effects of the socio-demographic variables in the logistic regression analysis are more likely to be due to patient misuse factors, as it seems unlikely that differences in prescriber behaviour would account for the differences in ORs between demographic subgroups, although this could potentially be possible.

Furthermore, while the explanatory variables explored in this research were found to be significant, it is likely that they explain a relatively small proportion of the variance in the dependent variables. Other factors such as patient attitudinal variables are likely to be more predictive for having leftover antibiotics and for antibiotic misuse in general. Such variables were not included in the survey questionnaire.

Chapter 7.

Literature Review

While there is a lack of literature with respect to antibiotic leftover behaviour specifically, broader antibiotic misuse literature has identified a number of socio-demographic factors that predict patient misuse more broadly. The findings of the survey analysis are discussed below in the context of broader academic literature.

7.1 Gender

The literature is generally unclear on whether gender is predictive of antibiotic misuse or misinformed attitudes. Some studies have found no significant association between sex and antibiotic use knowledge (Al-Shibani et al., 2017; Shehadeh et al., 2012). However, a Hong Kong study found that males were significantly more likely to report antibiotic misuse behaviours (You et al. 2008). In the study, females were almost half as likely to report engaging in antibiotic misuse than males were.

The findings from the survey analysis appear to support the findings of the Hong Kong study, showing that females are significantly less likely than males to have leftover antibiotics and significantly more likely to return leftovers to the pharmacy. Gender differences with respect to antibiotic misuse may therefore be dependent on nationality or culture, as studies from a variety of countries have found differing associations between gender and antibiotic misuse. Additional research may wish to examine this possibility in Canada.

7.2 Age

Age appears to be predictive of antibiotic misuse attitudes in the broader literature, with younger individuals being more likely to engage in antibiotic misuse than older individuals. Research has shown that individuals over the age of 30 were approximately twice as likely as those under 30 to know that antibiotics are not needed for common colds or the flu (Van et al., 2015). Individuals over 30 were also twice as likely to know that antibiotics are not typically needed for deep coughs or bronchitis.

Additionally, a Jordanian study found that younger participants were more likely to store antibiotics for future use and more likely to take antibiotics without a prescription than older participants (Shehadeh et al., 2012).

Thus, the literature supports the findings of this survey analysis, as age was a significant predictor for having leftover antibiotics. While the CCHS did not specifically ask questions regarding intent with respect to storing antibiotics for future use, it does suggest that younger Canadians are more likely to have leftover antibiotics from their prescriptions, increasing the likelihood that they may engage in other forms of misuse. Meanwhile, while older individuals such as seniors tend to require antibiotics more often due to deterioration of health associated with age, they appear to be more likely to follow their prescriptions properly.

7.3 Immigrant Status

Immigrant status is generally a risk factor for antibiotic misuse, although this varies significantly depending on country of origin. A New Zealand study found significant differences in reported misuse behaviours and AMR knowledge among a sample of Korean, Indian, and Egyptian immigrants (Norris et al., 2010). 71% of Korean immigrants reported that they would stop taking antibiotics once they felt better, rather than finishing the prescribed course as directed. 41% of Indian immigrants and 21% of Egyptian immigrants also reported doing so. Majorities of Egyptian and Korean respondents indicated that they would keep leftover antibiotics for future use; less than 20% of respondents in each group reported that they would return leftover antibiotics to a pharmacy, which is generally considered the appropriate method of leftover antibiotic disposal.

Additionally, a Greek study found that immigrants were nearly twice as likely as non-immigrants to answer incorrectly in a questionnaire regarding appropriate antibiotic use (Panagakou et al., 2012), and a study of Latin American immigrants in the United States indicated that 19% of individuals acquired antibiotics without a prescription, with 16% having transported nonprescribed antibiotics from another country (Mainous et al., 2005).

Therefore, the literature suggests that immigrants from certain regions in the world may be significantly more likely to engage in antibiotic misuse behaviours and less likely to be aware of antimicrobial misuse than non-immigrants. This is perhaps due to the fact that many countries have less robust antimicrobial stewardship programs than Western countries, with some countries having little to no public awareness of AMR and significantly more lenient antibiotic prescribing practices.

Since this survey analysis was not able to differentiate immigrants from country of origin, this may explain why the effect of immigrant status on leftover antibiotics in Canada was the opposite of what is found in the literature. Canada's immigrant profile is likely significantly different than the host countries included in these studies and could be an indication that many Canadian immigrants originate from countries with higher levels of AMR awareness than other origin countries. More research would be needed to determine this.

7.4 Education Level

Low educational attainment has also been shown to be a risk factor for antibiotic misuse in the broader literature. An American study surveyed participants and found that those whose education level was less than high school were approximately five times more likely than college-educated participants to believe antibiotics are needed for common colds and the flu (Van et al., 2015). Those who only completed high school were approximately twice as likely as college-educated participants to believe the same misconception. Similar findings were reported in other studies in Greece and Hong Kong as well (Panagakou et al., 2012; You et al., 2008).

The literature suggests that educational attainment is predictive of antibiotic misuse, with lower education level being associated with a greater chance of engaging in misuse and a higher education level being associated with a smaller chance of engaging in misuse. This association is also expected, as many AMR awareness initiatives are aimed at the public through schools. Individuals with low educational attainment may therefore not have been exposed to these awareness initiatives as often as their more educated counterparts.

However, educational attainment was not a significant predictor in the survey analysis. This may be due to AMR awareness potentially being roughly equal in Canada regardless of educational attainment. More research is needed in order to determine whether knowledge of AMR varies depending on general educational attainment, and if so, whether that translates to antibiotic misuse behaviours.

7.5 Household Income

Family income appears to be significantly associated with antibiotic misuse attitudes and behaviours, and this association is reported consistently throughout the broader literature. A study found that parents with low income were more likely to self-prescribe antibiotics for their children (Abobotain et al., 2013). Several other studies have found that higher family income was associated with more adequate patient knowledge of proper antibiotic use (Shehadeh et al., 2012; You et al., 2008). Parents with low income are also more likely to be associated with inadequate knowledge, inappropriate attitudes, and incorrect practices with respect to antibiotic use (Panagakou et al., 2012).

Like educational attainment, household income was also not a significant predictor in the survey analysis. However, educational attainment and household income are often strongly correlated and therefore including both variables in the logistic regression may have introduced multicollinearity effects, diffusing the effect of both variables on the dependent variables. Including just one of household income or educational attainment in the regression may have led to different results.

Chapter 8.

Policy Criteria, Measures, and Options

This chapter presents the key criteria and measures that are used to evaluate the benefits and drawbacks of the proposed policy options. A total of three policy options are presented and described in detail.

8.1 Policy Criteria and Measures

The criteria for this policy analysis include effectiveness, administrative complexity, cost, public acceptance, and healthcare professional acceptance. Table 3 displays a summary of these criteria, along with measures and indices for each. The broader literature and the findings from the survey analysis are used where possible to inform the evaluation of each policy option using these criteria.

Table 3. Policy criteria and measures

Criteria	Measure	Index
Effectiveness	The impact of the policy on decreasing antibiotic misuse	1 – Very small/no decrease in antibiotic misuse 2 – Small decrease in antibiotic misuse 3 – Moderate decrease in antibiotic misuse 4 – Large decrease in antibiotic misuse 5 – Very large decrease in antibiotic misuse
Administrative Complexity	The number of stakeholders and changes to management practices required to implement policy	1 – High complexity 2 – Moderate complexity 3 – Low complexity
Cost	Estimated annual budgetary costs to government associated with direct funding, materials, resources, and infrastructure	1 – High cost to budget 2 – Moderate cost to budget 3 – Low cost to budget
Public Acceptance	Acceptability to members of the general public	1 – Low acceptance 2 – Moderate acceptance 3 – High acceptance

Stakeholder Acceptance	Acceptability to healthcare professionals	1 – Low acceptance 2 – Moderate acceptance 3 – High acceptance
Total /17		

8.1.1 Effectiveness

The overarching objective is to reduce antimicrobial misuse in Canada in order to curb AMR. The findings of the survey analysis indicate that roughly 15% of Canadians who receive an antibiotic prescription report having leftover antibiotics, which increases the likelihood of future forms of misuse and can facilitate the spread of AMR. Thus, the policy’s expected effect on reducing patient misuse of antibiotics is considered when evaluating impact on antibiotic misuse.

Additionally, inappropriate antibiotic prescriptions can naturally increase the number of leftover antibiotics a patient has, particularly if a patient was prescribed antibiotics when they had a viral infection and recovered on their own shortly afterwards. Unnecessary antibiotic prescriptions also contribute to AMR by exposing bacteria to antibiotics when not required, thus increasing the likelihood of resistance developing. Unlike measuring leftover antibiotics, measuring the degree to which antibiotics are prescribed unnecessarily is more difficult and was not a component of the survey analysis. However, studies from comparable countries like the United States suggest that anywhere between 20% to 40% of antibiotic prescriptions are inappropriate (Chua, Fischer, & Linder, 2019; Olesen et al., 2018). Thus, the impact of the proposed policy on reducing over-prescribing practices from prescribers is also considered when evaluating a policy option against this criterion.

Effectiveness is scored on a 5-point scale that includes “no/very small decrease in antibiotic misuse,” “small increase in antibiotic misuse,” “moderate decrease in antibiotic misuse,” “large decrease in antibiotic misuse,” and “very large decrease in antibiotic misuse,” with larger decreases being scored higher. A 5-point scale is used to add additional weight to effectiveness in the analysis, given that the ability of a policy to reduce antibiotic misuse is the key objective of the policy.

8.1.2 Administrative complexity

How challenging a policy's implementation would be is another important consideration, with more complex interventions often more difficult for governments to coordinate and manage. The specific measure used for administrative complexity is the number of stakeholders that government must engage in outreach and coordination with as well as the number of governmental administrative changes required in order to implement a proposed policy, using a 3-point scale of "high complexity," "moderate complexity," and "low complexity" with low complexity receiving a higher score.

8.1.3 Cost

Budgetary impacts are also an important consideration when analyzing proposed stewardship policies. The measure for budgetary cost includes the annual costs to government of direct funding, or costs associated with the production of materials, resources, or infrastructure associated with a policy option, using a 3-point scale of "low cost to budget," "moderate cost to budget," and "high cost to budget," with lower costs receiving a higher score.

8.1.4 Public acceptance

The degree to which the general public will support or oppose the proposed policy is also considered in this analysis. Public acceptance is measured as the degree to which the public is expected to support the proposed policy, on a 3-point scale of "low acceptance," "moderate acceptance," and "high acceptance" with high acceptance scoring higher.

8.1.5 Stakeholder acceptance

The final criterion in this analysis is stakeholder acceptance. Specifically, the stakeholders considered under this criterion are healthcare professionals that are directly affected by the proposed policy. The measure for stakeholder acceptance is the degree to which healthcare professionals are expected to support the proposed policy, on a 3-point scale of "low acceptance," "moderate acceptance," and "high acceptance" with high acceptance scoring higher.

8.2 Policy Options

There are three proposed policies that are selected based on the results of the survey analysis and literature review. Each policy's key objective is to reduce antibiotic misuse, as detailed in section 9.1. The policies are described in detail below.

8.2.1. Option 1: Antimicrobial stewardship education programs

The first option is to develop comprehensive antimicrobial stewardship programs aimed towards educating both the general public as well as healthcare professionals and prescribers. Media campaigns would be employed across a variety of channels to raise general awareness of AMR, antimicrobial misuse, the importance of following prescriptions as directed, and the importance of returning leftover antibiotics to the pharmacy. As noted in the survey analysis and literature review, younger individuals are more likely to engage in antimicrobial misuse, so a targeted media campaign would primarily focus on social media in order to reach this demographic.

In addition to media messaging, educational programs and materials would be developed. These would include school programs that aim to educate children, adolescents, and young adults about AMR and antimicrobial misuse. The public awareness messaging in this option should focus on describing the public health threats of AMR; highlighting the fact that most infections do not require antibiotics; explaining the risks associated with failing to follow prescriptions as directed; and encouraging the public to return leftover antibiotics to the pharmacy if they happen to have leftover antibiotics. AMS campaigns tend to be particularly effective at changing knowledge and attitudes of parents and schoolchildren (Price et al., 2018), so outreach to schools would be included in this option. Educational programs and materials would also be developed for healthcare professionals, such as doctors, nurses, pharmacists, and dentists.

An existing program such as the "Do Bugs Need Drugs?" (DBND) program currently in place in British Columbia and Alberta can be used as a model for the scope of intervention, or it could be expanded to additional provinces if possible. The DBND program originated in Alberta in 1998 before expanding to British Columbia in 2005. It is considered the most comprehensive antimicrobial stewardship program in Canada. A total of 51,367 children, assisted-living residents, and healthcare professionals participated in the program between 2005 and 2011 (Mckay et al., 2011). The program utilizes public transit advertising campaigns, educational websites, social media campaigns, healthcare professional education sessions, public teaching sessions, print materials, and web applications for antibiotic prescribing guidelines to promote antimicrobial stewardship. It is administered in their respective provinces by the British Columbia Centre for Disease Control (BCCDC) and Alberta Health Services (AHS). The program leverages relationships with professional bodies such as Doctors of BC and the Alberta Medical Association to reach greater numbers of stakeholders and receives its funding from both provincial governments.

8.2.2. Option 2: Expanding pharmacist roles in patient medical homes

The second option is to expand pharmacists' roles in AMS through greater integration in patient medical homes (PMH) across Canada. PMHs are family practices in Canada that are designed to provide patients with longitudinal care using interprofessional teams of healthcare providers that are led by family doctors. Pharmacists receive extensive education and training with respect to prescribing practices for medications in Canada and therefore possess the appropriate expertise to play an important role in antibiotic prescribing and stewardship. However, many pharmacists in Canada report feeling underutilized in healthcare settings, and 61% cite lack of coordination with other healthcare professionals as a key barrier (Laliberte et al., 2012). Pharmacists' scope of practice activities vary depending on the province they practice in, and these practice activities can interact with antibiotic prescribing in both community and hospital settings. Such practice activities include the ability to renew/extend prescriptions, change drug dosages or formulations, and make therapeutic substitutions (Tannenbaum & Tsuyuki, 2013). Tighter integration of pharmacists in healthcare teams coupled with greater adoption of these practice activities could lead to additional structural checks along the antibiotic prescribing process, with pharmacists able to reduce an antibiotic prescription dosage if necessary or prescribe a more optimized antibiotic if physician prescriptions do not align with antibiotic prescribing guidelines.

More specifically, this option would aim to expand pharmacists' roles by promoting the inclusion of pharmacists in PMHs and hospitals with respect to antibiotic treatment and prescribing via outreach to provincial pharmacist/physician associations and colleges. Additional roles pharmacists would be encouraged to fill would include educating patients about AMR and appropriate prescription use when filling a prescription; encouraging the public to return leftover antibiotics to the pharmacy if they have leftovers; screening prescriptions to ensure adherence to prescribing guidelines; and communicating with their healthcare teams in PMHs with respect to antibiotic prescription modifications. Additionally, this option would involve dedicated funding for antimicrobial stewardship training practices in PMHs for pharmacists, physicians, and other practitioners in said healthcare teams in order to promote optimal coordination practices for managing antibiotic prescriptions. Dedicated funding would vary depending on a number of factors, including the size of the PMH and would need to be implemented within the existing payment models provinces use to fund PMHs (Ontario Ministry of Health, 2016).

8.2.3. Option 3: Improving AMR-AMU data linkage and accessibility

The third option is to establish a national integrated data network consisting of antibiotic prescription information in order to improve AMR and AMU surveillance systems in Canada. Currently, antibiotic prescription data in community settings such as doctor’s offices and walk-in clinics is difficult to access. Although roughly 75% of Canadian physicians now keep electronic medical records (Collier, 2015), much of antibiotic prescription data collected in community and hospital settings is siloed and fragmented. Existing national AMR-AMU surveillance systems, such as the Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS), rely on proprietary antibiotic prescription data purchased from IMS Canada – a private company that collects prescription data from retail pharmacies. CIPARS also currently does not link AMR-AMU between primary care settings and hospital settings and has limited data accessibility (Saxinger, Grant, and Patrick, 2014).

This policy option would pool antibiotic prescription data from participating primary care providers as well as hospitals into a centralized network which would then be used to provide comprehensive national and regional data on antibiotic prescribing practices. Ideally, electronic records from dentist offices would also be included under the scope of this option. This data could be used to address existing knowledge gaps with respect to antimicrobial use in Canadian communities, such as understanding the extent of antibiotic prescribing and the degree to which antibiotics are prescribed according to clinical guidelines. Data interpretation and regular reporting would also accompany the enhanced data linkage in this policy option, with reports stratifying prescription and resistance trends by demographics if feasible.

This data network would be modeled after the Danish Integrated Antimicrobial Resistance Monitoring and Research Programme (DANMAP), which links AMR and AMU data from both primary care settings and hospitals in order to publish annual reports that are accessible by researchers (Saxinger, Grant, and Patrick, 2014). The integration of prescription data from primary care settings would be modeled after the Canadian Primary Care Sentinel Surveillance Network (CPCSSN), which collects data on five chronic health diseases and three neurological conditions. CPCSSN health information is derived from electronic medical records in the offices of participating primary care providers, such as family doctors. The data is aggregated and protected such that all collection, retention, use, or disclosure of research data complies with privacy legislation.

Chapter 9.

Analysis of Policy Options

Each policy option is evaluated using the criteria and measures outlined in Chapter 8. Scores are summarized in Table 3 at the end of this chapter.

9.1. Analysis of Option 1: Antimicrobial Stewardship Education Programs

The effectiveness of antimicrobial stewardship education programs varies significantly, since stewardship programs can be implemented in a variety of ways and may differ in comprehensiveness. However, there is significant evidence that the DBND program has been effective at reducing antibiotic prescriptions since its inception. In British Columbia, annual antibiotic prescription rates have fallen 14% overall since the program was introduced in 2005 (BCCDC, 2019). The vast majority of this reduction is likely comprised of unnecessary antibiotic prescriptions that were avoided. It is also worth noting that before the DBND program was implemented, antibiotic prescription rates in the province had been increasing at an average annual rate of 0.8% between 2000 and 2005. If that trend were held constant, projected antibiotic prescription rates in British Columbia would have been roughly 21% higher in 2016 than they were in actuality. Thus, the DBND program seems to be significantly effective at reducing over-prescribing in the province and antimicrobial stewardship education programs modeled after it may see similar levels of success. Therefore, the impact of the policy option on reducing antibiotic misuse is scored 4/5.

A comprehensive antimicrobial education program that includes the key features of the DBND program is fairly complex from an administrative standpoint. Successful implementation of such a program involves coordination and planning with a variety of stakeholders, including public schools, health professional associations and colleges, community clinics, hospitals, and provincial departments. Federal support or funding may also add to the complexity of implementing this program nationwide. Thus, the administrative complexity of this policy option is judged to be high and scored 1/3.

The cost of implementing or expanding antimicrobial stewardship education programs varies depending on the scope of the programs and the existing infrastructure that a province already has in place to distribute programming. Using the DBND program as a model, the average cost of implementing and maintaining the DBND program, including printing educational materials, developing media campaigns, and hiring staff to deliver the training/education programs in British Columbia is $655,000 per year (Mamun et al., 2019), or roughly $0.13 per capita per year. Therefore, the cost of implementing this program in other provinces is assumed to be comparable, and the total cost would depend on the population size of the province. This is likely considered to be a low cost for provincial health budgets. The impact of the policy option on cost is scored as a 3/3.

Antimicrobial education programs are likely to be well-received by the general public. A national survey reported that 81% of Canadians indicated a desire for more government information on AMR (Leger, 2018) and therefore education programs and campaigns would help to meet this demand. Educational programs are also generally not burdensome for members of the public. Thus, public acceptance of this policy option is scored as a 3/3.

Acceptance from healthcare professionals may be somewhat less universal, as antimicrobial stewardship programs tend to place a relatively larger burden on physicians in the form of additional training in order to promote appropriate antibiotic prescribing. Therefore, healthcare professional acceptance of this policy option is scored as a 2/3.

9.2. Analysis of Option 2: Expanding Pharmacist Roles in Patient Medical Homes

A meta-analysis of 15 antimicrobial stewardship trials involving pharmacists were associated with a 4% reduction in overall antibiotic prescription rates over 6 months (Saha, Hawes, & Mazza, 2019), which is a relatively insignificant effect. However, when antimicrobial stewardship practices were implemented by pharmacists and physicians as part of a team, the antibiotic prescribing rate was reduced by 10%. Additionally, the rate of antibiotic prescriptions that adhered to general prescription guidelines increased by 14% when antimicrobial stewardship practices involved pharmacists and physicians operating as part of a team. Furthermore, an Australian study has indicated that patients who were provided with verbal education and direction on appropriate antibiotic prescription adherence by community pharmacists were significantly more likely to score higher on AMR knowledge tests (Northey, McGuren, & Stupans, 2014). This suggests that the impact of pharmacist intervention in antimicrobial stewardship practices can modestly decrease inappropriate prescribing as well as modestly increase AMR awareness. Thus, the effectiveness of this policy on reducing antibiotic misuse is scored as a 3/5.

Facilitating greater integration of pharmacists in PMHs would require some degree of outreach to professional physician/pharmacist associations and colleges. However, the administrative requirements for this initial outreach would likely be temporary, as the professional associations would eventually administer the antimicrobial stewardship initiatives to their members on their own. Furthermore, providing dedicated funding for antimicrobial stewardship training workshops in PMHs would require negotiating funding amounts on a case by case basis depending on the size of a given PMH. This would necessarily include administrative support from provincial health ministries and would add an additional component when bargaining with professional medical associations over broader payment agreements, which are renegotiated periodically. However, this is expected to represent a small additional administrative burden as these bargaining mechanisms are already in place. Therefore, the administrative complexity of this option is scored as a 3/3.

The direct incentive funding amounts for antimicrobial stewardship workshops for PMHs in this policy option would vary depending on the size of a given PMH, given that said training workshops would require larger funding amounts for PMHs with more physicians, registered nurses, and pharmacists. However, training programs of similar scope in Ontario have estimated costs of roughly $10,000/year for a FHT with 140,000 enrolled patients (Ontario Ministry of Health, 2018) or $0.07 per enrolled patient, with roughly 3 million patients enrolled in FHTs in the province in total. An estimated total cost of the proposed incentive funding for Ontario would be approximately $215,000/year. This funding total would of course vary from province to province based on the number of PMHs and staffing requirements. Because of the low estimated figures, the cost of this option is scored as a 3/3.

This policy option places no burden on the public, and patients generally report greater satisfaction when receiving primary care from integrated healthcare teams. However, increased scrutiny from both physicians and pharmacists with respect to antibiotic prescribing may slow down or delay the ability of members of the public to receive an antibiotic prescription in some cases, which may be a source of frustration – though this is not expected to present a significant delay. Public acceptance is therefore scored as a 3/3.

Given that there is incentive funding for antimicrobial stewardship training programs in this option, healthcare professional acceptance would likely also be high. Additionally, pharmacists have noted a greater desire for more active involvement in prescribing, given that they have reported feeling underutilized in primary healthcare settings when considering their education and training (Tannenbaum & Tsuyuki, 2013). Finally, many physicians have also noted a preference for working in PMHs as part of integrated teams of healthcare professionals; however, it is worth noting that there appears to be a generational divide among physicians, with younger physicians significantly more likely to prefer them than older physicians (Glauser, 2014). Therefore, the acceptance of this policy option among healthcare professionals is scored as a 2/3.

9.3. Analysis of Option 3: Improving AMR-AMU Data Linkage and Accessibility

Establishing a linked network of antibiotic prescription data from primary care providers would not intrinsically decrease the number of inappropriate antibiotic prescriptions, nor would it intrinsically reduce the proportion of leftover antibiotics resulting from appropriate prescriptions. However, improving regional and national surveillance of antibiotic prescriptions would enhance the implementation of other antimicrobial stewardship programs by providing the means to identify problematic prescribing trends in Canadian community settings. This option would therefore foster targeted policy interventions and investments – indirectly improving the effectiveness of initiatives designed to reduce antibiotic misuse. Thus, the effectiveness of this policy option at reducing inappropriate antibiotic prescriptions is scored as a 4/5, with the caveat that effectiveness would primarily be realized if this policy option is implemented in conjunction with existing AMR- or AMU-related initiatives.

This policy option would likely require expanding the administrative scope and capacity of existing surveillance bodies in Canada, with the most logical candidate being CIPARS. In order to successfully model the comprehensiveness of DANMAP, collection of prescription data from hospitals would need to be added to the community data currently collected by CIPARS. Additionally, significant stakeholder outreach and coordination would be required in order to collect data from primary care settings such as community clinics. Therefore, the score for administrative complexity of this policy option is scored as a 1/3.

The additional costs associated with this policy option would include largely be attributed to costs associated with establishing additional data linkage infrastructure and staffing required to maintain the network. However, these costs are not expected to be very significant, given that CIPARS already maintains and operates a significant data network with linkage capabilities to fulfill its current mandate. The cost of maintaining the DANMAP data network is reportedly $0.14 per capita per year (Sorensen, Lawrence, and Davis, 2014), which would equate to $5,262,600 per year if extrapolated to Canada’s population. Given that this policy option builds on existing CIPARS infrastructure, however, the incremental costs would likely be substantially lower. Costs could also be reduced if the data linkage infrastructure utilized for CPCSSN could be co-opted for the purposes of collecting AMR-AMU data from primary care medical records. The cost of this policy option is considered moderate and scored as a 2/3.

Establishing data linkages between existing AMR-AMU data sources and proposed primary care sources may present privacy concerns for the general public, as electronic medical records contain very sensitive information. However, existing databases that gather de-identified medical record data in Canada such as the CPCSSN have not seen any public backlash. Ensuring that the collection and use of this information is secure and meets privacy legislation as modelled by CPCSSN would help to mitigate these concerns. Therefore, public acceptance is scored as a 2/3.

Like with CPCSSN, healthcare professionals such as primary care physicians are not required to participate in the data sharing component of this option and therefore would not be burdened my implementation of this policy. Additionally, calls for increased AMR-AMU data accessibility and surveillance in Canada have been made by healthcare professionals and researchers (CIHR, 2016; Saxinger, Grant, and Patrick, 2014). Healthcare professionals' acceptance of this policy option is scored as a 3/3.

Table 4. Summary of policy evaluation

Criteria	Antimicrobial Stewardship Education Programs	Expanding Pharmacist Roles in PMHs	Improving AMR-AMU Data Linkage and Accessibility
Effectiveness /5	Large decrease in antibiotic misuse (4)	Moderate decrease in antibiotic misuse (3)	Large decrease in antibiotic misuse (4)
Administrative Complexity /3	High complexity (1)	Low complexity (3)	High complexity (1)
Cost /3	Low cost to budget (3)	Low cost to budget (3)	Moderate cost to budget (2)
Public Acceptance /3	High public acceptance (3)	High public acceptance (3)	High public acceptance (3)
Stakeholder Acceptance /3	Moderate stakeholder acceptance (2)	Moderate stakeholder acceptance (2)	High stakeholder acceptance (3)
Total /17	**13**	**14**	**13**

Chapter 10.

Recommendations

Given that the scope of addressing antimicrobial misuse is broad and requires multiple interventions in order to address, all three policy options analyzed above are recommended to be implemented. Additionally, all three options will likely offer complementary benefits when implemented together, likely leading to an overall effectiveness that is greater than the sum of its parts. Expanding pharmacist roles is recommended to be implemented first, as it can be implemented relatively quickly due to low costs and low administrative complexity, with the more onerous interventions such as the development of comprehensive AMS education programs and improving AMR-AMU data linkages following afterwards.

Comprehensive AMS education programs have been shown to be effective at reducing antibiotic misuse in a variety of jurisdictions, including jurisdictions within Canada. Stewardship programs designed for community physicians and the public are required to achieve a significant effect, as this combinatory approach addresses misuse in the form of over-prescribing as well as in the form of patient misuse. The DBND program in British Columbia and Alberta can be used as a model for the development of these stewardship programs in other provinces within Canada. If possible, expansion of the DBND program itself to other provinces should be explored, as its existing framework and infrastructure could accelerate the implementation of stewardship initiatives in other provinces. Some additional advantages of adopting AMS education programs include their relatively low costs and broad acceptance from both healthcare professionals and the public. However, a notable drawback of this option is the degree of outreach required to manage stakeholder networks and disseminate programs, materials, and other resources to healthcare professionals. In order to achieve a more targeted intervention, the findings of this analysis support the development of additional AMS educational materials and resources for dentists. Additionally, social media campaigns should be adopted in order to reach younger populations that are at greater risk of engaging in patient misuse. Implementation or expansion of AMS initiatives like the DBND program would largely fall on provinces, but the federal government could facilitate its adoption by assisting provinces in convening stakeholder groups or providing dedicated funding for AMS initiatives to provinces in order to offset provincial costs.

Expanding pharmacist roles in AMS would likely not be sufficient in order to meaningfully reduce antimicrobial misuse if adopted on its own due to its relatively narrow scope. This option does, however, have notable advantages; because of its narrow focus, it is the least costly intervention to implement while still maintaining a modest degree of effectiveness, thus making the policy relatively cost effective. This option also requires less outreach and administrative coordination than broader AMS stewardship initiatives like the DBND program and is likely to be accepted by both the public and healthcare stakeholders. Therefore, improving integration between pharmacists and healthcare teams such as PMHs can be implemented alongside broader AMS initiatives like the DBND program. Coupled with AMS education resources designed for physicians in the DBND program, elevating pharmacist roles can add an additional structural filter in the antibiotic prescribing process in many provinces that reduces the likelihood of inappropriate prescriptions being filled. Both initiatives combined would likely see a further reduction in antibiotic misuse, particularly over-prescribing, if used in conjunction with each other. If provinces wish to take immediate action to address antibiotic misuse, this policy could likely be implemented relatively quickly due to its low costs and low complexity, with broader AMS programs following afterwards.

Finally, improving AMR-AMU data linkage is also unlikely to be effective at reducing antibiotic misuse if implemented on its own. While increased prescription data and AMR data consolidation could directly lead to the development of useful benchmarks for hospitals, the primary effectiveness benefit of improving AMR-AMU data linkages is that it acts as a multiplier for other interventions. This option helps to support AMR-related research in Canada and can improve the efficacy of direct AMS interventions by uncovering problematic prescribing practices in the community; cross-referencing prescription practices with AMR rates; and identify concerning trends in geographic sub-regions. Additionally, the survey analysis indicates that surveillance is needed to identify concerning trends demographic sub-populations and that a comprehensive surveillance network should include prescription data from dentist offices as well as community clinics. This information can be used to inform more targeted AMS interventions and is therefore recommended to be implemented alongside AMS programs like the DBND program. Expansion of the existing CIPARS system should be modeled after the successful DANMAP surveillance program, and such an expansion can adopt the same framework and infrastructure that the CPCSSN system in Canada currently uses. However, it is worth noting some of the drawbacks of this option; this option is likely to be relatively complex administratively, as it requires significant coordination and merging of data from labs, hospitals, and provincial surveillance systems across the country. Additionally, there is a possibility that the public may have concerns with respect to the privacy of their medical information, so measures should be taken to ensure complicity with privacy legislation and data security practices.

Chapter 11.

Conclusion

With AMR becoming an increasingly serious public health threat, coordinated policy intervention is critical in order to curb the spread of drug resistance. This research has demonstrated the need for additional policy action to address antibiotic misuse in Canada. The findings from the survey analysis and literature review indicate that antibiotic misuse is common in the country, and that males and younger Canadians seem to be more likely to report having leftover antibiotics. Additionally, Canadians are more likely to report having leftover antibiotics when their prescription originated from dentist offices. These findings can be indicative of antibiotic misuse, although it is not clear if leftover antibiotics in this context are a result of patient misuse or over-prescribing/inappropriate prescribing; it is likely a combination of both. Thus, policy interventions should aim to address antibiotic misuse by targeting both manifestations.

The policy interventions recommended from this research include a combination of AMS initiatives as well as expanding AMR-AMU surveillance. Antibiotic misuse is broad in scope, and therefore policy action to mitigate it must be proportionately scoped as well. Coordination between provincial governments and the federal government is necessary in order to facilitate the implementation of the policies recommended in this analysis, but this level of coordination is also critical to address other AMR-related issues that fall outside the domain of human antibiotic misuse, such as antibiotic misuse in agriculture and incentivizing the pharmaceutical development of new antibiotics.

Further research on antibiotic misuse should examine metrics other than leftover antibiotics in order to paint a more complete picture of misuse in Canada. A better understanding of how much misuse can be attributed to prescriber behaviours versus patient behaviours can be used to tailor policy action further. In addition, future research should aim to analyze provincial and regional AMU contexts as well in order to potentially identify sub-regions with problematic resistance/misuse trends. Survey questionnaires should also be designed with participant AMR knowledge in mind. Asking participants directly if they follow a prescription appropriately is unlikely to garner a valid response, as participants often do not know what it means to take a prescription adequately. Finally, while demographic characteristics can play a role in understanding antibiotic misuse, future research should aim to better understand the attitudinal factors that influence misuse among prescribers and patients in Canada, as well as the role that structural characteristics of healthcare systems can play in addressing antibiotic misuse.

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Appendix A.

2018 CCHS Rapid Response – AMU Questions

Table A.1. List of 2018 CCHS AMU questions and response categories

CCHS Question Code	Question/Response
AMU_Q005	In the past 12 months, have you been prescribed any oral antibiotics? 1: Yes 2: No 8: RF 9: DK
AMU_Q010	In the past 12 months, were you prescribed more than one (oral antibiotic)? 1: Yes 2: No, just one 8: RF 9: DK
AMU_Q020	(Thinking about this last oral antibiotic), was it prescribed at a...? 1: Walk-in clinic or doctor's office 2: Hospital as an outpatient (e.g., emergency ward or day clinic) 3: Hospital while you were admitted 4: Dentist's office 5: Another place 8: RF 9: DK
AMU_Q025	(Thinking about this last oral antibiotic) did you, or someone on your behalf, receive information from a health care professional, including a pharmacist, on how to take it? 1: Yes 2: No 8: RF 9: DK
AMU_Q030	(Again, thinking about this last oral antibiotic), did you take it as prescribed? 1: Yes (took it as prescribed) 2: No (did not take it as prescribed) 3: Not applicable (did not get prescription filled)) 4: Still taking it 8: RF 9: DK

CCHS Question Code	Question/Response
AMU_Q040	In the past 12 months, thinking of all the oral antibiotics you were prescribed, did you have any left? 1: Yes 2: No 8: RF 9: DK
AMU_Q045	What did you do with them? 1: Threw them in the garbage 2: Flushed them down the toilet / sink 3: Kept them / did nothing 4: Gave them to someone else for their use 5: Returned them to the pharmacy 6: Other action 8: RF 9: DK

Appendix B.

Sample Characteristics

Table B.1. Sample Description Statistics

CCHS Variable Code	Variable/Response Category	Proportion of sample
DHHSEX	**Gender**	
	Male	49.3%
	Female	50.7%
INCDVHH	**Household Income**	
	$0 to $9,999	1.9%
	$10,000 to $19,999	4.3%
	$20,000 to $29,999	5.9%
	$30,000 to $39,999	7.0%
	$40,000 to $49,999	7.1%
	$50,000 to $59,999	7.0%
	$60,000 to $69,999	7.0%
	$70,000 to $79,999	6.2%
	$80,000 to $89,999	5.6%
	$90,000 to $99,999	5.2%
	$100,000 to $149,000	20.9%
	$150,000+	22.0%
EHG2DVR3	**Educational Attainment**	
	Less than secondary school graduation	17.3%
	Secondary school graduation, no post-secondary education	21.4%
	Post-secondary certificate diploma or university degree	59.5%
SDC_IM3	**Immigrant Status**	
	Yes	24.1%
	No	74.5%

Appendix C.

Raw Logistic Regression Outputs

Table C.1. Outputs for reporting leftover antibiotics.

Survey: Logistic regression

Number of obs	=	5,027
Population size	=	5,760,766
Replications	=	1,000
Design df	=	1,000
F(6, 995)	=	8.56
Prob > F	=	0.0000

amu_leftover	Observed Odds Ratio	Bstrap * Std. Err.	t	P>|t|	[95% Conf.	Interval]
sex	.5981887	.1011408	-3.04	0.002	.4292833	.8335513
age	.9801456	.0040824	-4.81	0.000	.9721673	.9881895
immigrant	.6364534	.1161814	-2.48	0.013	.4448316	.9106208
education2	.7976159	.132259	-1.36	0.173	.5760741	1.104356
persincome	.9673115	.0272356	-1.18	0.238	.9153157	1.022261
amu_place2	1.496462	.2580213	2.34	0.020	1.066898	2.098981
_cons	.8880207	.2811007	-0.38	0.708	.4771455	1.652705

Table C.2. Outputs for reporting returning leftovers to pharmacy.

Survey: Logistic regression

Number of obs	=	5,027
Population size	=	5,760,766
Replications	=	1,000
Design df	=	1,000
F(6, 995)	=	8.56
Prob > F	=	0.0000

amu_leftover	Observed Odds Ratio	Bstrap * Std. Err.	t	P>|t|	[95% Conf.	Interval]
sex	.5981887	.1011408	-3.04	0.002	.4292833	.8335513
age	.9801456	.0040824	-4.81	0.000	.9721673	.9881895
immigrant	.6364534	.1161814	-2.48	0.013	.4448316	.9106208
education2	.7976159	.132259	-1.36	0.173	.5760741	1.104356
persincome	.9673115	.0272356	-1.18	0.238	.9153157	1.022261
amu_place2	1.496462	.2580213	2.34	0.020	1.066898	2.098981
_cons	.8880207	.2811007	-0.38	0.708	.4771455	1.652705